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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,854	01/22/2004	Mark David Fidock	PC10959B	8327

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PATENT DEPARTMENT, MS8260-1611
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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,854	FIDOCK, MARK DAVID	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 09/14/2004.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/023,775.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence alignment

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group IV, claims 15-18 in the reply filed on September 14, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Applicants' preliminary amendment filed on September 14, 2004 has been entered. Claim 16 has been canceled. Claims 15, 17, and 18 have been amended. Claims 1-15 and 17-21 are pending. Claims 15, 17, and 18 are under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional applications 60/260,590 (filed on 01/09/2001) and 60/296,660 (filed on 06/07/2001).

Acknowledgment is also made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been received in application 10/023,775.

Drawings

4. The drawings filed on 01/22/2004 are accepted by the Examiner.

Rejections—35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 15, 17, and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 15, 17, and 18 are drawn to a method for identifying a compound that binds to and activates or inhibits the polypeptide of SEQ ID NO: 2. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not requires further research.

The invention is based upon the discovery of PFI-019 nucleic acid sequence by bioinformatics analysis. The specification asserts that PFI-019 nucleic acid sequence encodes a encoding a G-protein coupled receptor whose ligand is likely to be a nucleotide or a nucleotide derivative and that the PFI-019 polypeptide is most similar to P2Y1 receptor (page 17; Fig. 2). The specification shows PFI-019 polypeptide activation by 2-chloro-ATP, 2-methyl-thio-ATP, 2-methyl-tho-ADP, and UTP in a FLIPR cell-based assay (Example 4; Figures 3-6). Nonetheless, the

specification fails to show the specific biological functions or any physiological significance of the PFI-019 polypeptide or nucleic acid. It has been well documented that UTP is an inactive agonist for P2Y1 receptor (Harden et al, Annu. Rev. Pharmacol. Toxicol. 35: 541-579, 1995; Ayyanathan et al, BBRC. 218 :783-788, 1996 ; Bhagwat et al, Eur. J. Med. Chem. 32:183-193, 1997; King et al, TIPS, 19 :506-514, 1998 ; Kugelgen etal, Naunyn-schmiedeberg's Arch Phamacol. 362: 310-323, 2000). However, the specification discloses that UTP is a very potent agonist of the polypeptide and is nearly 10 times as potent as 2-methyl-thio-ATP or 2-chloro-ATP (Fig. 3-6). This contradiction clearly provides evidence that further research is needed to establish the biological functions of the polypeptide of the present invention.

The specification asserts that the present invention provides agonists and antagonists of the polypeptides of the present invention, which are useful in treatment of a list of numerous diseases (page 6 of the specification). However, these asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the polypeptides or nucleic acids of the present invention nor any diseases that are associated with the molecules of the present invention. Clearly, further research would be required to determine the functions of the claimed molecules or to identify a disease that can be treated or diagnosed with the claimed molecules See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966),

noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The specification further asserts the utilities of polynucleotides as primers or hybridization probes (page 12, 4th paragraph). The specification also asserts that the present invention provides methods for identifying compounds that bind to and activate or inhibit the polypeptide of PFI-019 (SEQ ID NO: 2). However, such uses are all considered research uses only designed to identify a particular function of the claimed molecules and are not a substantial utility. See, e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." Moreover, such uses are not specific to the instant molecule but applicable to any GPCR polypeptides or nucleic acid molecules.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The assertion that the claimed nucleic acid encodes the polypeptide of PFI-019 that is similar to P2Y receptors (page 17) does not endow the claimed nucleic acids with a specific and substantial utility because members of P2Y receptors have diverse structures and biological functions (see, e.g., Harden et al, Annu. Rev. Pharmacol. Toxicol. 35: 541-579, 1995; Bhagwat et al, Eur. J. Med. Chem. 32:183-193, 1997) and the functions of each P2Y receptor need to be determined individually. No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the compounds.

7. Claims 15, 17, and 18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if the claimed methods were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 17 and 18 recite a method for identifying a compound that binds to and/or inhibits activation of the polypeptide of SEQ ID NO: 2 comprising contacting a detectable first *nucleotide or nucleotide derivative* known to bind to and activate said polypeptide. However, other than 2-chloro-ATP, 2-methyl-thio-ATP, 2-methyl-tho-ADP, and UTP, the specification does not provide sufficient guidance and information regarding the structural requirements commensurate in scope with what is encompassed by the instant claims. It is unpredictable whether a nucleotide, for example CTP, or a nucleotide derivative, binds to the polypeptide of PFI-019 of SEQ

ID NO: 2 because there is no structural limitation recited in the claims. As noted above, the art teaches that UTP is an inactive agonist for P2Y1 receptor (Harden et al, Annu. Rev. Pharmacol. Toxicol. 35: 541-579, 1995; Ayyanathan et al, BBRC. 218 :783-788, 1996 ; Bhagwat et al, Eur. J. Med. Chem. 32:183-193, 1997; King et al, TIPS, 19 :506-514, 1998 ; Kugelgen etal, Naunyn-schmiedeberg's Arch Phamacol. 362: 310-323, 2000). However, the specification discloses that UTP is a very potent agonist of the polypeptide and is nearly 10 times as potent as 2-methyl-thio-ATP or 2-chloro-ATP (Fig. 3-6). This contradiction underscoes the fact that undue experimentation is required to practice the claimed methods because one skilled in the art would have to make the nucleotides and their derivatives before the methods can be carried out.

Furthermore, claims 15, 17, and 18 recites the amino acid sequence encoded by the cDNA of NCIMB Deposit No. 41101. Applicants' referral to the NCIMB Deposit No. 41101 on page 14 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is

required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

Accordingly, the disclosure fails to enable such a method for identifying a compound that binds to and/or inhibits the polypeptide of SEQ ID NO: 2 comprising contacting a nucleotide or nucleotide derivative known to bind to said polypeptide. It would require undue experimentation for one skilled in the art to make and use the genus of the nucleotide or nucleotide derivative and thus the instantly claimed methods.

Claim Rejections—35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 15 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional

characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 15 and 18 are are drawn to methods for identifying a compound that binds to and/or inhibits activation of the polypeptide of SEQ ID NO: 2 comprising contacting a detectable first *nucleotide or nucleotide derivative* known to bind to and activate said polypeptide. Thus, the claims are drawn to a method comprising contacting a genus of structurally undefined nucleotides and their derivatives.

However, the specification fails to provide the critical structural features to adequately describe the genus of nucleotides and nucleotide derivatives that may be used in the claimed method. The specification merely discloses 2-chloro-ATP, 2-methyl-thio-ATP, 2-methyl-tho-ADP, and UTP, which activates the polypeptide of SEQ ID NO: 2 in a FLIPR cell-based assay (Example 4; Figures 3-6). There is no defined relation between function and structure of nucleotides and nucleotide derivatives. There is even no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing structural characteristics, the specification does not provide adequate written description of the genus of nucleotides and nucleotide deritives.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize

that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleotides and nucleotide derivatives, and therefore conception is not achieved until reduction to practice has occurred. Therefore, only the methods for identifying a compound that binds to and/or inhibits activation of the polypeptide of SEQ ID NO: 2 comprising contacting 2-chloro-ATP, 2-methyl-thio-ATP, 2-methyl-tho-ADP, and UTP, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections—35 USC § 112, 2nd paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because it recites "a membrane preparation of said cells". It is unclear whether applicants intend to recite a preparation of the polypeptide of SEQ ID NO: 2 or a membrane preparation that does not necessarily comprise the polypeptide of SEQ ID NO: 2. For example, in E. coli cells, the majority of the polypeptide would be present in inclusion bodies.

Claim Rejections—35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 15, 17, and 18 are rejected under 35 U.S.C. §102(e) as being anticipated by Ramakrishnan (WO200214511 A2, International Publication Date: 21 February 2002; 102 (e) date: 14 August 2000).

Ramakrishnan teaches a human P2Y1-like G-protein coupled receptor with the amino acid sequence being 100% identical to SEQ ID NO: 2 and the nucleic acid encoding the receptor. The nucleic acid encoding the receptor is identical to the polynucleotide set forth in SEQ ID NO: 1 (see attached sequence alignment). Ramakrishnan teaches that ATP is a likely ligand of the receptor (see, e.g., top of page 10 and bottom of page 57). Ramakrishnan also teaches various binding assays (39) and functional assays (page 43) using either a purified P2Y1-like GPCR polypeptide, a cell membrane preparation or an intact cell (lines 12 to 14 of page 43). In binding assays, either the test compound or the P2Y1-like polypeptide can comprise a detectable label (lines 25-26 of page 39).

In Example 1 and 3, Ramakrishnan teaches radioligand binding assays. Specifically, membrane preparation are incubated in the presence of ^{125}I-labled ligand or test compound. The binding affinities of different test compounds are

determined in equilibrium competition binding assays by measuring radioactivity ^{125}I-labled ligand or test compound.

Ramakrishnan teaches that the human P2Y1-like GPCR is expected to bind a ligand to produce a signal, such as cyclic AMP formation, mobilization of intracellular calcium, or phosphoinositide metabolism (top of page 10; Examples 4-6). At the bottom of page 43, Ramakrishnan teaches that a screening assay may be used to screen for a compound that inhibits activation of the receptor polypeptide by contacting cells expressing the P2Y1-like polypeptide with both a receptor ligand and a test compound. Inhibition of the signal generated by the ligand indicates that a test compound inhibits activation of the receptor. Ramakrishnan further teaches the screen method may be employed for identifying a test compound which activates the receptor by contacting such cells with a test compound and determine whether each test compound generates a signal, i.e., activates the receptor.

Therefore, the reference of Ramakrishnan teaches meets the limitations of claims 15, 17, and 18.

Conclusion

14. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00

pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
November 28, 2004